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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/441,411	11/16/99	SCHOLLER N	730033.409

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EXAMINER	
BAKER, A	
ART UNIT	**PAPER NUMBER**
1632	10

DATE MAILED: 01/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

1- File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/441,411	SCHOLLER ET AL.	
	Examiner	Art Unit	
	Anne M. Baker	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2000*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☒ The proposed drawing correction filed on *16 November 1999* is: a)☐ approved b)☒ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7*.
18)☐ Interview Summary (PTO-413) Paper No(s) _____
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1632. Contact information for the Examiner now handling this application is noted below.

The amendment filed October 17, 2000 (Paper No. 9) has been entered. Claims 1-8 have been amended.

Claims 1-8 are pending in the instant application.

The following rejections are reiterated and constitute the complete set of rejections being applied to the instant application. Rejections and objections not reiterated from the previous Office Action are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 3-8 of the previous Office Action mailed 4/12/00 (Paper No. 5), because the specification, while being enabling for a vaccine for eliciting or enhancing the titer of antibodies for Her2/neu protein, wherein the vaccine comprises individual expression constructs which each recombinantly express Her2/neu, murine B7.2

or murine 4-1Bb ligand, does not reasonably provide enablement for any vaccine for eliciting or enhancing the titer of antibodies for any cell surface receptor antigen, wherein the vaccine comprises one or more recombinant expression constructs which express (either as individual expression vectors, a single expression vector, or a combination thereof), any cell surface receptor antigen plus two immune response altering molecules, consisting of any accessory cell agent and any T cell agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants argue that the specification provides support for a wide variety of cell surface receptor antigen vaccines, including teachings directed to selection of suitable cell surface receptor antigens (SRAs) and immune response altering molecules (IRAMs). However, the claimed vaccine is comprised of one or more expression constructs. Thus, gene delivery with subsequent gene expression at a level and location appropriate to elicit the desired response is a critical aspect of the invention. Furthermore, as the design and development of this type of vaccine is inherently unpredictable, one skilled in the art would not be able to produce similar vaccines for other SRAs.

Applicants point out that Example 2 used FVB/N-TgN(MMTVneu) mice, not nude mice as alleged in the previous Office Action. The Examiner is aware of this and accepts Applicants arguments that appropriate animal models are sufficient to demonstrate a pharmaceutical effect. The scope of enablement described above was indicated with this consideration in mind. This example is critical to the enabled scope of the invention.

Applicants further argue that the claimed invention is enabled because the specification provides details regarding how to construct a vector for gene delivery and how to effectively deliver a gene. However, the details provided are sufficient only to enable the scope as indicated. Given the unpredictability with

regard to gene delivery and the *in vivo* effects of a gene once delivered, undue experimentation would have been required to extend the teachings in the specification to other SRAs. Ample evidence has been provided regarding the unpredictability of gene therapy as described by Eck et al. (1996),

Applicants argue that a person having ordinary skill in the art of molecular biology can take any known protein encoding gene and place it in an expression vector, with only routine, not undue, experimentation. Applicants go on to discuss a wide variety of expression vectors known in the art. However, this is not sufficient to enable the claimed invention, as the claimed invention is directed to a vaccine which must elicit a particular effect with regard to antibody titer and must provide a protective effect, as that is the function of a vaccine. The production of such effects *in vivo* by gene delivery means is highly unpredictable and undue experimentation is required to produce the desired effect.

Applicants disagree with the Examiner's contention that gene therapy is unpredictable. Applicants argue that there is the implied assertion in the Office Action that applicants must provide human gene therapy data. On the contrary, if that were the case, no scope of enablement would have been indicated. The Examiner has clearly accepted the results obtained in the mouse tumor model as evidence of enablement for the scope indicated. Applicants further argue that the Examiner is asserting that the claimed invention lacks utility. Again this is not the case, as no scope of enablement would have been indicated if the invention lacked utility. The Examiner has accepted Applicants assertion that the compositions can be used for gene delivery to provide a protective effect. This is a credible utility. Once Applicants' asserted utility is accepted as a credible utility, the Examiner then has the duty to assess enablement based on this asserted utility. A scope of enablement was indicated. No utility rejection was made, nor would one be appropriate where a scope of enablement is found. Applicants further argue that "[i]n no case has a Federal court required an applicant to support an asserted utility with data from human clinical trials." Again, human clinical trials are

not required; the Examiner has already accepted the mouse tumor model as evidence of enablement for the indicated scope.

Applicants assert that Eck et al. makes sweeping generalizations and tells only one side of the story with regard to gene therapy. Applicants argue that there are dozens of clinical trials in the U.S. that involve the use of gene therapy. However, clinical trials are not evidence of the routine nature of gene therapy, but rather represent further research intended to determine whether or not a particular protocol works. Furthermore, intensive effort has been directed to the development of such protocols with minimal success.

Applicants argue that Blaese et al. (1995) successfully used gene therapy to treat ADA deficiency. However, those skilled in the art do not refer to this as a success story. Verma et al. point out that the patient is still treated with PEG-ADA, and the authors emphasize that the efficacy of gene therapy **cannot be evaluated** until patients are completely taken off alternative therapies, such as PEG-ADA in this case (p. 242, column 1, paragraphs 2 and 3). If it was a simple matter to take the vectors used in ADA gene therapy (a trial initiated in 1990) and, with routine experimentation, apply the technique to the treatment of other diseases, many successful gene therapy protocols would already exist. However, this is not the case. Applicants cite Roth et al. (1996) as evidence of successful gene targeting. However, the references cited by Applicants and the Examiner are clear evidence that intensive effort has been applied to the development of gene therapy protocols with minimal success. None of the gene therapy methods that Applicants point to were developed using routine experimentation.

Applicants cite additional gene therapy references including Khuri et al. (2000), Cavazzana-Calvo et al. (2000) and Kay et al. (2000). It is well-established that the invention must be enabled at the time of filing. The filing date for this application is 11/16/99. The references cited were published after the filing date of this application and do not constitute evidence that only routine experimentation was required to enable the

instant invention. Further, these references do not relate to antigen vaccines as claimed. Thus, the teachings do not evidence enablement of the claimed vaccines.

Applicants refer to the reference of Crystal (1995) which discusses successful human gene transfer. However, gene transfer does not equate with gene therapy because the *in vivo* effect manifested upon gene delivery is unpredictable. This reference does not describe successful therapy.

The references cited by Applicants do not constitute evidence that only routine experimentation is required for the development of gene therapy protocols. The references clearly indicate that, in each instance, intensive investigation was required to develop experimental protocols.

Conclusion

No claim is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Baker whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached on (703) 305-6608. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-8724.

Questions of formal matters can be directed to the patent analyst, Kay Pinkney, whose telephone number is (703) 305-3553.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne-Marie Baker, Ph.D.

Scott D Priebe

SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER